EFFECT OF TIGHT GLYCAEMIC CONTROL ON POST-OPERATIVE INFECTION IN DIABETICS WITH RAISED GLYCOSYLATED HAEMOGLOBIN

A DISSERTATION SUBMITTED AS PART FULFILMENT FOR
M.D DEGREE BRANCH X (ANAESTHESIA) EXAMINATION
DR.M.G.R MEDICAL UNIVERSITY OF TAMILNADU
FEBRUARY/MARCH 2008

CERTIFICATE

This is to certify that the dissertation entitled **"EFFECT OF TIGHT GLYCAEMIC CONTROL ON POST-OPERATIVE INFECTION IN DIABETICS WITH RAISED GLYCOSYLATED HAEMOGLOBIN"** is a bonafide work of **Dr.Kamal Kumar** in partial fulfillment of the requirement for the M.D degree (Branch X) Anaesthesiology Examination of The Tamil Nadu Dr.M.G.R Medical University, Chennai, to be held in February / March 2008.

Dr.Verghese T Cherian
Professor and Guide,
Department of Anaesthesiology,
Christian Medical College &
Hospital, Vellore.

Dr. Manickam Ponniah,
Professor and Head,
Department of Anaesthesiology,
Christian Medical College &
Hospital, Vellore.

ACKNOWLEDGEMENT

This thesis was an eye opener for me into the world of “clinical research” and I could not have done it without the able guidance and assistance of

Dr. Verghese T Cherian, Professor in Anesthesiology, Christian Medical College and Hospital, Vellore.

I am grateful to **Dr. Manickam Ponniah**, Head of the Department of Anaesthesia, Christian Medical College and Hospital, Vellore for his valuable support and guidance throughout this endeavor.

I thank my colleagues in Anaesthesia, nursing staff of our general surgical ward for their co-operation and encouragement.

I would like to thank my statistician **Mr. Solomon Christopher** who helped me in my statistical analysis.

Last but not least I thank god for his grace to complete this study

CONTENTS

AIM AND OBJECTIVES

To study the effect of tight glycaemic control on posy-operative infection in diabetics with raised glycosylated haemoglobin

1. To measure the incidence of post-operative infection in diabetics and to analyze its correlation with the level of glycosylated haemoglobin. (**clinical audit**)
2. To compare the effect of restricting the post-operative blood glucose < 140 mg.dL-1 to the existing practice of maintaining it < 200 mg.dL-1 on post-operative infection, in diabetics with glycosylated haemoglobin more than 7%. (**interventional clinical trial**)

INTRODUCTION

Patients with diabetes mellitus have been shown to have a higher incidence of peri-operative morbidity and mortality compared to those without diabetes, which is attributed to hyperglycaemia. (1, 2) There is substantial evidence to suggest that mean blood glucose levels >200-230 mg.dL-1 is associated with increased risk of infection. (1, 3, 4) The widely followed practice is to maintain the plasma glucose below 200 mg.dL-1, in the post-operative period. (1) However, has been shown that 'tight' control of blood sugar at 80-110 mg.dL-1 reduces the morbidity and mortality further, but this was achieved in an intensive care unit setting, and required frequent monitoring of blood sugar level to avoid hypoglycemia. (5)

Some authors have suggested that the effect of chronic hyperglycaemia may also contribute to post-operative morbidity. (1, 6, 7) The level of glycosylated haemoglobin (HbA1c) reflects the control of blood glucose in the previous 8-12 weeks. (8) A clinical audit of 490 diabetics undergoing elective surgery demonstrated that those with HbA1c greater than 7% had a higher incidence of surgical site infection. (9)

This study is an effort to answer the question, whether maintaining a tighter control of blood sugar in the immediate post-operative period, in patients with HbA1c > 7%, reduces post-operative infection.

REVIEW OF LITERATURE

Diabetes mellitus:

Diabetes mellitus is a disease characterized by hyperglycemia resulting from either a deficiency of insulin or resistance to its action. According to the American Diabetes Association (ADA), the criteria for the diagnosis of diabetes are the presence of symptoms of diabetes such as polyuria, polydipsia and unexplained weight loss along with a casual plasma glucose more than 200 mg.dL-1 (11.1 mmol.L-1); or a plasma glucose more than 126 mg.dl-1 (7.0 mmol.L-1) after a period of no caloric intake for 8 hours. (10) The ADA defines good glycaemic control as pre-prandial plasma glucose between 90–130 mg.dL-1, post-prandial plasma glucose less than 180 mg.dL-1 and a glycosylated haemoglobin (HbA1c) level less than 7%. These levels are also recommended for patients admitted in the hospital. (10, 11)

Diabetics are at increased risk for premature morbidity and mortality associated with vascular, renal, retinal, and neuropathic complications due to long standing hyperglycaemia. (12, 13) Hyperglycaemia is also associated with short-term complications such as ketoacidosis and hyperosmolar coma, intracellular dehydration, electrolyte imbalance (decreased sodium, potassium and phosphorous), decreased phagocytosis and delayed immunologic and

lymphocytic activity. (14, 15)

Diabetes and Surgery:

A diabetic patient is said to have 25 % chance of undergoing surgery during his lifetime. This is due to the increase in the incidence of atherosclerosis and related complications like ischemic heart disease, peripheral vascular disease along with micro vascular complications leading to retinopathy, neuropathy, and nephropathy. (16)

The incidence of peri-operative morbidity and mortality among diabetic patients is higher when compared to non-diabetics,(17,18) but better monitoring and control of peri-operative blood glucose have shown a decline.(20,29) During peri-operative period the goal is to maintain the plasma glucose levels that minimize the risk for hypoglycemia but that are low enough to prevent post-operative morbidity.

The various recommendations for the ideal level of plasma glucose, during the peri-operative period are 120-200 mg.dL-1 (19,20,21,22,23), 125-180 mg.dL-1, < 150mg.dL -1 (8.3mmol.L-1) following cardiac surgery (1) and the most recent being to aim as close to 110 mg.dL-1 in a critical care unit (5,10) and 90-130 mg.dL-1 in a general ward. (10, 11) Most authors would agree that glucose level should be maintained below 200 mg.dL-1.

There is evidence to suggest that in-hospital hyperglycemia is associated with adverse outcomes**.** A meta-analysis of 14 studies has shown that hyperglycemia (blood glucose >140 mg.dL-1) with or without a prior diagnosis of diabetes increased both in-hospital mortality and congestive heart failure (CHF) in patients admitted for acute myocardial infarction (2).

Similar data were reported in a prospective study of 336 patients. Hyperglycemia (fasting blood glucose >126 mg.dL-1, random blood glucose >200 mg.dL-1 in general medical and surgical units was associated with an 18-fold increase in in-hospital mortality, a longer length of stay , more subsequent nursing home care, and a greater risk of infection (3) .

Diabetes and Surgical site infection:

A diabetic patient is at greater risk during the post-operative period to systemic and surgical site infection and they are also prone to metabolic decompensation, such as fluctuating blood glucose levels and keto-acidosis. (1, 14, 24) The association between hyperglycemia and the susceptibility to surgical site infection is multi-factorial.

i) Hyperglycemia has been shown to impair the normal functions of the neutrophils, which include adherence, chemotaxis, phagocytosis and intracellular bactericidal activity. The degree of neutrophil impairment correlates with the degree of hyperglycemia. The glucose level threshold for neutrophil dysfunction is 200 mg.dL-1 (range - 130-275 mg.dL-1). (1)

ii) Hyperglycemia alters vascular permeability and the normal redox reactions which creates a state of pseudo-hypoxia and impaired tissue defenses. Elevated tissue levels of glucose and the formation of oedema due to the increased vascular permeability, promotes bacterial growth. (1)

iii) Micro- and macro-vascular manifestations of diabetes may disrupt supply of nutrients, oxygen, leukocytes and antibiotics to the operated site leading to impaired wound healing. (1) Oxygen is necessary for macrophage mobility and growth of granulation tissue.

iv) In patients with diabetic neuropathy, disruption of the skin may go undetected which can form a portal for entry of the bacteria. (1)

v) Glucose is a pro-inflammatory mediator that has been shown to stimulate cytokine

production and inhibit endothelial nitric oxide levels. Insulin enhances the ability of cytotoxic lymphocytes to attack target cells. (1) Therefore, insulin deficiency makes the diabetic patients more susceptible to infection.

vi) The bone marrow-derived endothelial progenitor cell is vital in vasculogenesis and wound healing, but their numbers are decreased in diabetes due to impaired activity of endothelial derived nitric oxide synthetase. (25, 26, 27) Poor healing of diabetic wounds is characterized by impaired angiogenesis and vasculogenesis. Control of blood sugar level also retards the progression of vascular complications.

Latham *et al* (6) studied the association of glucose control with surgical site infections among patients undergoing cardio-thoracic surgery. In a prospective cohort and case-control study, to assess the importance of diabetes, diabetes control, hyperglycemia, and previously undiagnosed diabetes in the development of surgical-site infections. They found that presence of diabetes and post-operative hyperglycaemia were independently associated with development of surgical site infection.

Rossini *et al* (14) reviewed various studies suggesting a relationship between metabolic abnormality and the diabetic complications. They divided the complications of uncontrolled diabetes into two major categories – short term and long term. The short term complications are ketoacidosis with hyperosmolar coma, intracellular dehydration, electrolyte imbalance, decreased phagocytosis, reduced immunologic and lymphocyte activity, and impaired wound healing. The long term complications are nephropathy, neuropathy, retinopathy, cataract formation, perinatal mortality and those due to vascular disease. They suggested that until the question of degree of control of diabetes can absolutely be resolved, the recommendation should be that the blood glucose level be controlled as close to the normal as possible.

Stephen H, *et al* (13) did a retrospective cohort study to determine the impact of diabetes mellitus on short-term mortality and morbidity in patients undergoing coronary artery bypass surgery. They found that the 30-day mortality was 3.7% in patients with diabetes and 2.7% in those without. Morbidity, infections and the composite outcomes occurred more commonly in diabetic patients and were associated with a risk about 35% higher in diabetics than in non-diabetics. They concluded that diabetes is an important risk factor for mortality and morbidity among those undergoing coronary artery bypass surgery. They concluded that more research was needed to determine if better peri-operative glycaemic control improved outcome.

Bhatia *et al* (28) did a prospective study to evaluate the risk factors for postoperative wound infection in 615 patients undergoing coronary artery bypass graft surgery, of whom 269 (43%) were diabetic. 116 (18.86%) patients developed infection of the surgical sites involving sternum (75%), leg (21.3%) and forearm (3.44%). Sternal site, obesity, diabetes mellitus and female gender were associated with significantly higher infection rates. Diabetes, especially uncontrolled, was a significant risk factor for the development of surgical site infection.

Golden *et al* (1) studied the peri-operative glycaemic control and the risk of infections complications in 411 diabetics, who underwent coronary artery surgery. Peri-operative glycaemic control was assessed by the average of six capillary glucose measurements taken during the 36 hour following surgery. The major outcomes studied were infections of the leg and the chest wounds, pneumonia and urinary tract infection. They found that patients with higher mean capillary glucose readings were at increased risk of developing infections compared with those with the low post-operative glucose levels. They concluded that in diabetics who undergo coronary artery surgery, hyperglycemia is an independent predictor of short-term infections in the post-operative period, and the physician should consider a glucose concentration target of <200 mg.dL-1 to reduce the risk of infection.

Glycaemic control in immediate post-operative period:

Zerr *et al* (4) investigated the occurrence of wound infection in a cohort of 1,585 diabetics who underwent cardiac surgery. There was a strong correlation of risk of wound infection with the mean concentration of blood glucose on the first postoperative day. It increased from 1.3% among patients with glucose level between 100-150 mg.dL-1, to 6.7% among those with levels of 250-300 mg.dL-1.

McAlister *et al* (29) studied 291 diabetic patients undergoing coronary artery bypass graft surgery, to explore the association between glycaemic control and in-hospital morbidity and mortality. They found that hyperglycaemia > 200 mg.dL-1, on the first post-operative day, was associated with adverse outcome.

Gandhi *et al* (30) conducted a retrospective observational study of consecutive adult patients who underwent cardiac surgery to estimate the magnitude of association between intra-operative hyperglycemia and peri-operative outcome. They concluded that intra-operative hyperglycemia is an independent risk factor for complications, including death, after cardiac surgery.

Hyperglycemia is an independent predictor of infection in patients with diabetes undergoing cardiac surgery. (1,24) Furthermore, hyperglycemia in the first 48 post-

operative hours was associated with a two-fold higher rate of surgical site infection among patients undergoing cardiothoracic surgery compared with those who were normoglycaemic. (6)

Kim *et al* did a retrospective study on 329 diabetic patients who had undergone lumbar spine surgery. Of these 152 had undergone the surgery before the implementation of a protocol wherein an infusion of insulin was used during the peri-operative period to maintain the blood glucose below 200 mg.dL-1. They demonstrated that the deep wound infection was significantly lower in patients who were operated after the initiation of the protocol to control the blood glucose level in the immediate post-operative period. (7)

Glycaemic control in critically ill:

Many interventional studies have linked reversal of hyperglycaemia to better clinical outcomes in medical and surgical situations, especially following acute myocardial infarction, cardiac surgery and in critically ill patients. (36)

In a study of critically ill, medical-surgical intensive care unit patients, the use of insulin therapy to achieve blood glucose levels of 80–110 mg.dL-1, reduced mortality by 34%, sepsis by 46%, renal failure requiring dialysis by 41%, blood transfusion by 50% and critical illness poly neuropathy by 44% . Van den Berghe *et al* demonstrated that strict post-operative blood glucose control not only reduced morbidity, but also reduced mortality by as much as 42%. (5)

Krinsley *et al* (32) evaluated the effect of administering insulin infusion for better glycaemic control on patients admitted to a medical-surgical ICU and compared the outcome with a historical control group. The study group had improved blood glucose levels (130.7 vs. 152.3 mg/dl) and significant reduction in mortality and median length of ICU stay. (32)

A meta-analysis of clinical trials evaluating the effect of insulin therapy on mortality in hospitalized patients with critical illness showed that insulin therapy decreased short

term mortality by 15% in a variety of clinical settings. (33**)**

Insulin and glycaemic control:

The advent of insulin revolutionalised the treatment(35,36,37) of diabetic patients undergoing surgery. The mortality of diabetics undergoing foot amputations was 50% in the 1930's, 32.8% in the 1940's, 22% in the 1950's, 9% in the 1970's and today it is no different from non-diabetics undergoing the same procedure. (34)

Rassias *et a*l (35) tested the effect of an insulin infusion on neutrophil function in diabetic patients scheduled for coronary artery bypass surgery and found that a continuous insulin infusion and glucose control during surgery improved white cell function and may increase resistance to infection after surgery.

Lazer *et al* (36) did a study to determine whether tight glycaemic control in diabetic coronary artery bypass graft patients would improve peri-operative outcome. One hundred forty-one diabetic patients undergoing cardiac surgery were prospectively randomized to either tight glycaemic control (125 - 200 mg.dL-1) or standard control (250 mg.dL-1) using intermittent subcutaneous insulin before induction of anaesthesia and continuing for 12 hours after surgery. Patients in the tight glycaemic control group had a lower glucose level

(138 mg.dL-1 versus 260 mg.dL-1), a lower incidence of atrial fibrillation (16.6% versus 42 %) and a shorter post-operative length of stay (6.5 versus 9.2 days). Patients with tight glycaemic control also showed a higher survival over the initial 2 years after surgery with decreased episodes of recurrent ischemia (5 % versus 19 %) and had fewer episodes of wound infections.

Furnary *et al* (4) compared the impact administering insulin by continuous infusion to the previous practice of intermittent subcutaneous injections in diabetics undergoing cardiac surgery. Insulin infusion during the peri-operative period reduced the risk of deep sternal wound infection by 57%.

Glycosylated Haemoglobin:

Glycosylated haemoglobin (HbA1c) is a term used to describe a series of stable minor hemoglobin components formed slowly from haemoglobin and glucose. The rate of formation of HbA1c is directly proportional to the glucose concentration (38). Since erythrocytes, with a life-span of 120 days, are freely permeable to glucose, the level of HbA1c in a blood sample provides a glycaemic history of the previous 2-3 months. Laboratory measurement of HbA1c became available in the late 1970s.

HbA1c is formed non-enzymatically by haemoglobin's exposure to plasma glucose. This

simple reaction proceeds in two stages (Fig 1).

1. Glucose combines with the amino group of the valine residue at the N-terminus of 18 goblin chains to form an aldimine compound (Schiff base). This reaction is reversible, and dissociation back to haemoglobin and glucose can occur readily.

2. Internal rearrangement of the aldimine intermediate by the amadori reaction yields a stable ketoamine derivative, which is irreversible.

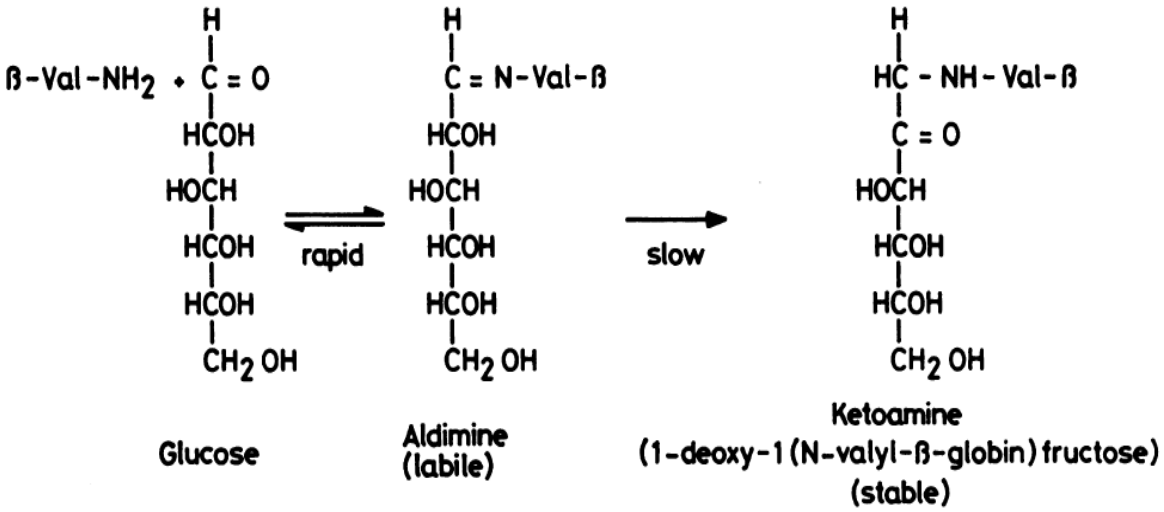

Fig. 1 *Reactions leading to the formation of haemoglobin* A_{1c}.

Glycosylation begins during erythropoiesis and continues slowly throughout the lifespan of the circulating haemoglobin.

As each erythrocyte circulates for 120 days, there is opportunity for late maillard

reactions or non-enzymatic browning to occur (the products of these reactions are referred to as Advanced Glycation Endproducts [AGE]) and the extent of these changes appear to correlate with the level of HbA1c. In connective tissues and vascular endothelium, AGEs may be important mediators of diabetes pathology as well as the normal aging process. AGE accumulate in diabetes as a result of hyperglycemia, leading to glycosylation of collagen. This process results in abnormal collagen, which is highly inflexible and prone to breakdown, particularly over pressure areas. Research has shown that several biochemical pathways associated with hyperglycemia, including glucose auto-oxidation, polyol pathway, prostanial synthesis, and protein glycation can increase the production of free radicals. (39) Free radicals generated by the auto-oxidation reactions of sugar and sugar attached to protein are possible sources of oxidation stress and damage to protein in patients with diabetes. Glyco-oxidation products accumulate in collagen at an accelerated rate in patients with diabetes. (40) This oxidative stress leads to complications in diabetes, such as tissue damage and cell death, which are reversed by antioxidants. Anti-oxidants such as vitamin C and E can lower HbA1c levels, possibly by inhibiting glycation. Renal and hepatic diseases, haemolytic anemia and haemoglobinopathies shorten red cell survival and therefore the period of exposure to glucose, leading to a decrease in HbA1c.

Hennesse *et al* (41) investigated the interaction of blood glucose concentration and wound collagen glycosylation, collagen content, and proteolytic activity during wound

healing in diabetic rats. They showed that long term hyperglycemia leads to the formation of AGE, which contributes to many of the complications of diabetes. The amount of AGE is proportional to the duration of diabetes. AGE leads to abnormal cross linking causing increased phagocytosis of the affected proteins and protein catabolism. This increased catabolism of structurally abnormal proteins in uncontrolled diabetic patients leads to impairment of wound healing.

One percent increase in glycosylated haemoglobin has been shown to be associated with 18% increase in the risk for coronary heart disease or stroke and a 28% increase in the risk for peripheral vascular disease. (42) These data highlight the utility of the glycosylated haemoglobin level as a measure of risk for cardiovascular events in type 2 diabetes.

Khaw *et al* (43) correlated the level of HbA1c to the incidence of cardiovascular events. They demonstrated a 21% increase in cardiovascular events for every 1% increase in HbA1c level above 5%. They also concluded that HbA1c level of 6.59% in a non-diabetic predicts a higher cardiovascular risk than a HbA1c level of 5.5% in a well-controlled diabetic. These two studies (42, 43) have clearly proved that the glycosylated haemoglobin level is an independent risk factor for cardiovascular events, regardless of diabetes status.

Bishop *et al*(46) examined the effect of HbA_{1c} level on surgical site infection in 32 diabetic patients undergoing penile prosthetics surgery and found that the incidence of infection was higher in those with a $HbA_{1c} > 11.5\%$. However, few years later, these observations were refuted by Wilson *et al* (47) who studied 114 diabetic patients undergoing penile prosthetic surgery. They compared wound infection in those with HbA_{1c} greater and less than 11.5% and did not find any correlation between HbA_{1c} and surgical site infection.

Latham et al (6) analyzed 300 diabetic patients undergoing cardiac surgery and compared wound infection in patients with HbA_{1c} greater and less than 8%. They concluded that elevated HbA_{1c} was not associated with statistically significant increase risk of infection. However, the poorly controlled diabetics had significantly higher levels of blood glucose in the post-operative period.

Dronge *et al* (9) did a retrospective observational study on the relationship of long-term glycaemic control and pos t-operative infection in 490 diabetics. Oral treatment was the main form of diabetic therapy (59.0%). The HbA_{1c} levels ranged from 4.6% to 15.5% (median - 7.3%). The incidence of infection in patients with $HbA_{1c} <7\%$ was 12% while it was 20% in those with $Hba_{1c} > 7\%$. They concluded that good pre-operative glycaemic control (HbA_{1c} below 7%) reduces post-operative infections following a variety of surgical procedures.

Pilot Study (A Clinical Audit)

All diabetic patients scheduled for major elective surgery over a period of six months were included in the audit. The patients were followed up till time of discharge.

The following were recorded:

1. Glycosylated hemoglobin levels
2. Blood glucose levels (pre-, intra-, and post- operative)
3. Surgical wound site and other systemic infections
4. Metabolic derangements such as hypoglycemia and ketoacidosis
5. Duration of hospital stay

A total of 50 patients were included in the audit over the six month period. They were grouped into those with HbA_{1c} more than or less than 7%. Those with HbA_{1c} <7% had a better glycaemic control before, during and after the surgery. Those with HbA_{1c} >7% had wider fluctuations in glucose levels. The incidence of wound infection in those with HbA_{1c} >7% was **30%** which was significantly (**p- 0.023**) higher than in those with HbA_{1c} <7%. The duration of hospital stay was also significantly more in the higher glycosylated haemoglobin group.

Table1. Comparison between two groups:

	HbA1c > 7%	**HbA1c < 7%**	**P value**
Number	30	20	
Age (years)	53.2 ± 11.9	55.2 ± 10.7	0.502
Weight(kg)	62.1 ± 11.4	64.7 ± 15.8	0.493
HbA1c (%)	8.6 ± 1.47	6.3 ± 0.41	0.000 *
Preoperative sugars	164.4 ± 44.5	119.5 ± 31.3	0.000 *
Intra-operative sugars	144.7 ± 36.9	127.7 ± 18.6	0.005 *
Post-operative sugars			
Day 1	238 ± 82.9	178 ± 55.1	0.0009*
Day2	228 ± 60.9	171 ± 80.8	0.0004*
Day 3	237 ± 86.9	174 ± 80.6	0.000*
Day 4	225 ± 54.0	174 ± 70.6	0.0002*
Day 5	182 ± 67.9	176 ±41.4	0.0685*
DAY 6	201 ± 56.8	147 ± 53.8	0.0000*
Complications			
Wound infection	9	1	0.023*
Hypoglycemic attacks	10	3	0.004
Myocardial infarction	0	1	0.312
Hospital stay	6.9 ± 5.12	5.5 ± 1.76	0.048

The patients were regrouped into those who developed wound infections in the post-operative period and those who did not, and the data was reanalyzed. Those with wound infection had a higher level of HbA1c and blood glucose in the post-operative period. (Table 2)

Table2. Regrouped based on postoperative wound infection:

Wound infection Without wound infection P value Number 10 40 Pre-operative sugars (mg.dL-1) 163 ± 51 146 ± 38.0 0.0275 Intra-operative sugars(mg.dL-1) 140 ± 46.4 140 ± 25.2 0.54 Post-operative sugars (mg.dL-1)			

The question which remained unanswered was whether tighter glycaemic control in the post-operative period would reduce the incidence of infection in those with $HbA_{1c} > 7\%$.

Patients and Methodology

Approval was obtained from the institutional research and ethical committee before starting the clinical trial. All diabetic patients, with glycosylated haemoglobin (HbA_{1c}) of more than 7%, scheduled for elective surgery, were eligible to be enrolled in this study. Patients with preoperative infection were excluded. These patients were explained about the study by the anaesthesiologist the evening before the surgery and a written consent was obtained from the volunteers.

All medications, including oral hypoglycemic drugs (except for metformin) were administered the evening before the surgery. The patients were fasted for six hours prior to surgery and allowed clear fluids up to two hours before surgery. On the day of the surgery, oral hypoglycaemic drugs and insulin were omitted. Blood glucose was measured just before induction of anaesthesia.

All the patients received a standard general anaesthetic technique using midazolam, fentanyl, thiopentone, and vecuronium for induction, and maintained with morphine, oxygen, air and isoflurane.

Intra-operative Glycaemic Control:

During the intra-operative period the blood glucose was measured every hour by 'Accu-chek' glucometer. The aim was to maintain the blood glucose below 140 mg.dL-1. An infusion of insulin (actrapid ®) in a concentration of 1 unit per ml was administered depending on the measured blood glucose. (Table 3)

Table 3: Variable Insulin Regimen:

BLOOD GLUCOSE	**INSULIN INFUSION**
<70mg.dL-1	Stop insulin. Give 100ml of 5% dextrose Over 10min. Do blood glucose after 15 min
70 -100mg.dL-1	stop insulin and do blood glucose after 30 min
100 – 150mg.dL-1	Insulin infusion 1 unit.hr-1. Do blood glucose after1 hr
150 – 200mg.dL-1	Give one unit bolus and start infusion 2units.hr-1. Do blood glucose after 1hr
200 – 250 mg.dL-1	Give 2 units bolus and infusion 3 units.hr-1. Do blood glucose after 1hrs.
250- 300mg.dL-1	3units bolus and 4 units.hr-1 .Do blood glucose after 1hrs.
300 - 350mg.dL-1	Give 4 units bolus and start infusion 4units.hr-1. Do blood glucose after 1 hr
350 – 400 mg.dL-1	Give 4 units bolus and start an infusion 5 units.hr-1 .Do blood glucose after 1hr

At the end of the surgery, the patient was allocated into one of the following groups, based on a randomization table, for management of blood glucose in the post-operative period.

Group A – Tight Glycaemic control (<140 mg.dL-1)

Group B – Standard Glycaemic control (<200 mg.dL-1)

Blood glucose monitoring and management of the patients in group B was done by the respective surgical unit doctors, as per the current standard of care, in the institution, for diabetic patients in the post-operative period. All these patients were administered 5% dextrose at the rate of 100ml per hour with 5-8 units of neutral insulin (Actrapid®) added to each pint. The aim was to maintain the blood glucose below 200mg.dL-1. If the blood glucose exceeded 200mg.dL-1, 6 units of Actrapid® were injected subcutaneously. The blood glucose was monitored every 4 – 6 hours.

The management of those in Group A was as follows. Five units of neutral insulin (actrapid®) were added to each pint of 5% dextrose and infused at 100 ml per hour. An infusion of neutral insulin (actrapid®) as was started during the surgery, was continued during the postoperative period to maintain a blood glucose < 140 mg.dL-1. Insulin infusion rate was titrated as per the variable

insulin regime (Table 3) according to the blood glucose level, which was measured every 2 hours. This mode of management was maintained for three postoperative days or till the patients started normal diet. During this period, the investigator was available on call and could be paged for any queries or problems.

The patients were followed up till the day of discharge from the hospital. Any complications during this period, such as surgical wound infection, re-explorations, fever, signs of respiratory or urinary tract infections, or sepsis were closely observed for and recorded. The duration of hospital stay was noted. The primary physician was asked to report if the patient returns within a month with signs of infection.

Wound infection was defined as the presence of sero-sanguinous or purulent discharge from the surgical site or wound dehiscence.

Sepsis was defined as temperature more than 370C with associated tachycardia, tachypnoea and a positive blood culture. Urinary tract infection was considered if the patient had fever, dysuria and a growth >1,00,000 .ml-1 of bacterial colonies on urine culture. Blood glucose below 60 mg.dL-1 was documented as hypoglycaemia. Proforma is shown as Appendix.

SAMPLE SIZE

The Clinical Audit demonstrated that the incidence of post-operative wound infection in diabetic patients with HbA_{1c} level > 7% was 30% (P1). The hypothesis of the clinical trial was to show if maintaining the post-operative glucose level below 140 mg.dL-1 would reduce wound infection to less than 5%.

$$N = \frac{2PQ\ \{Z1 - \alpha/2 + Z1\text{-}\beta\}\ 2}{(P1 - P2)2}$$

$$P = \frac{P1+P2}{2} = \frac{30+5}{2} = \frac{35}{2} = 17.5$$

$$Q = 100 - 17.5 = 82.5$$

$Z1\text{-}\alpha = 1.96$: $Z1\text{-}\beta = 0.84$ (α=5%; 1-ß = 80%)

$$P1 - P2 = 30 - 5 = 25$$

$$N = \frac{2 \times 17.5 \times 82.5\ \{1.96+0.84\}2}{625}$$

$$N = \frac{19894}{625} = 36$$

Statistical Analysis:

The basic structure of the analysis was a comparison of two groups of patients undergoing major elective surgery with high glycosylated haemoglobin. The major outcome event was the blood glucose control during the post-operative period and the development of surgical wound infection. Using the summary statistic approach, the average value of the blood glucose was calculated for each patient. Independent test was performed over the summary statistic to find the difference in mean. Base line and postoperative outcome variables were compared with the use of Pearson's chi-square test. The analysis was done using 'SPSS for Windows' version11 software.

RESULTS

Fifty diabetic patients with glycosylated haemoglobin greater than 7%, scheduled for elective surgery, were consented for the study. The preoperative and intra-operative management of all the patients were similar. At the end of the surgery, they were randomly allocated into one of the two groups to decide the glycaemic control during the post-operative period. The plasma glucose level of those in the Study Group was aimed below 140 mg.dL-1, while for those in the Control Group was aimed below 200 mg.dL-1, as is the standard practice in this institution. All the patients were managed in the general ward.

Demographic Data:

The patients in both the groups were comparable with respect to age, weight, duration of diabetes, level of HbA1c, and the fasting blood glucose on the day of surgery (**Table 4**).

Glycaemic control:

During the intra-operative period, the blood glucose was measured every hour for all the patients while during the post-operative period, it was measured every 2 hours for those in the Study Group and every 4 - 6 hours for those in the Control Group. The mean blood glucose during the intra-operative period and for each post-operative day was calculated for each patient, and compared between the groups (**Table 5**). There was no

statistically significant difference between the preoperative and the intra-operative blood glucose between the two groups. However, the blood glucose was significantly higher in the Control Group on the first five post-operative days.

Morbidity and Mortality:

Table 6 shows the comparison of morbidity and mortality in the study and the control group. Thirteen (44%) patients in the 'Control' group developed infection compared to only one (4%) in the 'Study' group. In the 'Control' group, 7 (28%) patients developed wound infection while only 1 (4%) patient in the 'Study' group had wound infection. This was statistically significant (p-0.023). The incidence of respiratory tract infection was also higher in the 'Control' group.

The incidences of hypoglycemic episodes were comparable in the two groups. The hospital stay was prolonged in the' Control' group (10.5 days) compared to the 'Study' group (8 days), but it is not statistically significant. One patient in the study group died due to leakage from the bowel anastomosis leading to sepsis.

Factors affecting Wound Infection:

The characteristics of those patients who developed surgical site infection were compared with those who did not (Table 7). The blood glucose levels were significantly higher during the surgery and during the first three post-operative days, in those who had surgical site infection. The duration of diabetes was longer in those who had infection, although not statistically significant. Patients with surgical site infection had a longer hospital stay.

Table 4 - Patient demography:

	Study Group (Tight Glycaemic Control)	**Control Group (Normal Glycaemic Control**	**p value**
Number of patients	25	25	
Age (years)	51.6 ± 8.6	54 ± 7.1	0.402
Male: Female	13: 12	9: 16	
Weight (kg)	66.7 ± 11.3	65.8 ± 10.2	0.491
Duration of diabetes (years)	6.4	6.16	0.667
HbA1c (%)	8.38 ± 0.96	8.5 ± 1.5	0.089
Pre-operative glucose	143.9± 36.1	146.8 ± 36.7	0.587
Type of surgery			
Intra-abdominal	7	4	
Superficial	15	17	
Cardio-Vascular	3	4	

Table 5: Blood Glucose levels

	Study Group (Tight Glycaemic Control) n=25	**Control Group (Normal Glycaemic Control) n=25**	**p value**
Preoperative glucose	143.9 ± 36.15	146.8 ± 36.7	0.587
Intra-operative glucose	126.0 ± 25.3	139 ± 31.9	0.08
Post-operative			
Day 1	136.0 ± 17.1	220 ± 48.3	0.000 *
Day 2	134.9 ± 16.1	209 ± 36.1	0.000 *
Day 3	139.1 ± 26.7	194 ± 35.2	0.000 *
Day 4	160.2 ± 48.0	185 ± 32.7	0.027 *
Day 5	145.2 ± 36.8	160 ± 31.7	0.049 *
Day 6	171.9 ± 53.8	160.2 ± 46.0	0.719
Day 7	166.3 ± 57.8	157 ± 45.8	0.696

Table 6: Post-operative morbidity and mortality

	Study Group (Tight Glycaemic Control) n=25	**Control Group (Normal Glycaemic Control) n=25**	**p value**
Infections	**1 (4%)**	**11 (44%)**	

	Surgical site infection	1 (4%)	7 (28%)	0.02 *
	Respiratory infections	0	5 (20%)	0.018 *
	Urinary tract infections	0	1 (4%)	0.312
Hypoglycaemia		3 (12%)	1 (4%)	0.29
Death		1 (4%)	0	0.312
Hospital stay (days)		8.0 ± 3.4	10.5 ± 5.6	0.212

Table 7: Comparison between patients with and without wound infection

	With wound infection	Without wound infection	p value
Number of Patients	8	42	
Age	55.6 ± 8.7	52.6 ± 8.0	0.719
Weight	71 ± 12.6	64.9 ± 10.1	0.312
Pre-operative glucose (mg.dL-1)	157.5 ± 36	143 ± 36.0	0.194
Intra-operative glucose (mg.dL-1)	166.8 ± 35.7	126.5 ± 23.3	0.001*
Post-operative glucose (mg.dL-1)			
Day 1	210 ± 39.5	171 ± 56.6	0.039*
Day 2	206.5 ± 36.5	165 ± 45.7	0.012*
Day 3	199.3 ± 39.9	160 ± 39.2	0.018*
Day 4	195.5 ± 44.17	167 ± 41.0	0.100
Day 5	164.8 ± 55.4	150 ± 27	0.645
Surgery duration (minutes)	226.8 ± 89	215 ± 135.8	0.412
HbA1C (%)	8.55 ± 0.9	8.52 ± 1.3	0.364
Hospital stay (days)	13.3 ± 4.1	8.52 ± 4.5	0.010
Duration of Diabetes (years)	8.87 ± 7.0	6.0 ± 4.0	0.244

DISCUSSION

It is widely accepted that patients with diabetes are at higher risk of developing infections and other post-operative complications. This is attributed to the short-term effect of hyperglycaemia on the immune function, pathogen growth and vascular permeability and also its long-term effect on microvasculature and tissue proteins.(1) The usual line of management of diabetic patient is directed towards the glycaemic control which can be acutely brought under control by intensive insulin therapy. However, it is a well established fact that chronic exposure to high glucose level leads to glycosylation of proteins and collagen leading to poor wound healing.(41) The level of glycosylated haemoglobin (HbA1c) may be taken as a surrogate measure of the glycosylation of the tissues. Although, the American Diabetes Association has recommended a HbA1c < 7% as a measure of good diabetic control, (10) this investigation is frequently not measured or ignored.

The purpose of this study was an attempt to answer two questions -

a) Do diabetics with HbA1c greater than 7 % have a higher incidence of post-operative infection?

b) In diabetics with HbA1c > 7 %, can a tighter glycaemic control in the peri-operative period decrease the incidence of post-operative infection?

To answer the first question, a prospective clinical audit was done on all diabetic patients undergoing major surgery, over a six month period. Those with HbA1c >7 % had a significantly higher incidence of surgical site infection. The previous studies (46,

47, 6) which have addressed this issue could not demonstrate this correlation, perhaps due to the fact that they segregated the patients at a higher level of HbA1c (11.5% and 8%). The American Diabetes Association considers good glycaemic control with HbA1c <7 %, and hence it was the criteria chosen for this study. However, the peri-operative blood glucose showed wide fluctuations, perhaps a reflection of uncontrolled diabetes. Similar findings have being demonstrated in a recently published retrospective audit (9), but the difference in the incidence of wound infection between the two groups was not significant.

This clinical audit formed the basis of the investigative clinical trial to answer the second question. The standard protocol, in this institution, to manage post-operative diabetic patients in the general ward is to monitor the blood glucose, using Accuchek®, every 4-6 hours and to administer insulin subcutaneously if the blood glucose exceeds 200 mg.dL-1. This is a trade-off between preventing the glucose to exceed the widely accepted level for increased post-operative complications (1) and the dreaded complication of hypoglycaemia in a poorly supervised, general ward.

In the study group, the aim was to maintain the blood glucose < 140 mg.dL-1. Although, various recommendations exist, a meta-analysis of 14 studies has shown that blood glucose >140 mg.dL-1 with or without a prior diagnosis of diabetes increased both in-hospital mortality and congestive heart failure.(2) A tighter control of blood glucose in the post-operative period would have required more frequent monitoring to detect hypoglycaemia. This would raise the issues of finances, the feasibility in a poorly

supervised, busy general ward and the morbidity of an undetected hypoglycaemic event. The pre-operative and intra-operative blood glucose levels were comparable between the two groups, but the mean blood glucose over the five post-operative days was significantly lower in the study group. The incidence of surgical site and respiratory infection (44%) was significantly higher in the control group, which reflected in prolonged hospital stay.

In most clinical settings, the peri-operative management of diabetics is based on the pre-operative blood glucose levels. However, the clinical audit has shown (**Table 1**) that even with good pre-operative and the intra-operative glycaemic control, the rate of surgical site infection is higher among those with HbA1c >7 %. This would suggest that acute hyperglycaemia can be controlled but the residual effects of chronic hyperglycaemia may linger on. A significant finding in the audit as well as the clinical trial was that the mean glucose level during the first three post-operative days in those who developed wound infection was above 200 mg.dL-1. Therefore, it seems that the effect of chronic hyperglycaemia may be offset by tight glycaemic control over the initial 3-5 days after surgery. This study has tried to answer the commonly faced dilemma among physicians managing diabetic patients with reasonably well-controlled blood glucose but raised glycosylated haemoglobin.

Limitations of the study

The sample size of 36 for the ‘clinical trial’ was based on the clinical audit, wherein the incidence of surgical site infection was 30%. The duration of the clinical trial was for

one year, and the number of diabetics with HbA1c > 7 % scheduled for elective surgery was only 50. Therefore, the study findings of these 50 patients (25 in each group) were analysed, which has shown statistical significance.

Conclusion

Diabetics with glycosylated haemoglobin more than 7 % have a high incidence of surgical site infection and other complications in the post-operative period which can be reduced by maintaining a mean glucose level below 140 mg.dL-1 during the initial 3 – 5 post-operative days.

BIBLIOGRAPHY

Golden SH, Peart-Vigilance CP, Kao WH, Brancati FL. Peri-operative glycemic control and the risk of infectious complications in a cohort of adults with diabetes. *Diabetes Care.* 1999;22:1408-1414,

1. Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. *Lancet.* 2000;355:773-778.

2. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *Journal of Clinical Endocrinology Metabolism* 2002;87:978-982.

3. Zerr KJ, Furnary AP, Grunkemeier GL, Bookin S, Kanhere V, Starr A: Glucose control lowers the risk of wound infection in diabetics after open heart operations. *Annals of Thoracic Surgery;* 1997; 63:356–61.

4. Van Den Berghe G, Wouters P, Weekers F,. Intensive insulin therapy in critically ill patients. *New England Journal of Medicine* 2001; 345:1359–1367.

5. Latham R, Lancaster AD, Covington JF, Pirolo JS, Thomas CS. The association of diabetes and glucose control with surgical site infections among cardiothoracic surgery patients *Infecton Control Hospital Epidemiology* 2001; 22:607-612.
6. Kim BO, Kim SW, Lee MS, ShinH, Relationship of Glucose Control and Wound Infection in Diabetics after lumbar Spine Surgery. *Journal of Korean Neurosurgery Society* 2005; 37:44-47.
7. Gerstein HC, Glycosylated hemoglobin: finally ready for prime time as a Cardiovascular risk factor, *Annals of Internal Medicine* 2004;141: 475-6
8. Dronge AS, Melissa F. Perkal, Kancir S, Concato J, Aslan M, Ronnie A. Rosenthal, Long term Glycemic Control and Postoperative Infectious Complications. *Archive of Surgery*. 2006; 141:375-380 .
9. Standards of medical care in diabetes-2007. *Diabetic Care*. 2007; 30: S4-41.
10. Inzucchi ES, Management of Hyperglycemia in the Hospital Setting: *The New England Journal of Medicine* 2006; 355:1903.
11. Stratton IM, Adler AI, Neil NAW, Matthews DR, Association of glycaemia with macro vascular and micro-vascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *British Medical Journal* 2000; 321: 405-412.

12. Stephen H. Schneider Jeffrey L. Carson, Peter M. Scholz, Anita Y. Chen, Eric D. Peterson, Jeffrey Gold , Diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery .*journal of American. College of Cardiology.* 2002; 40:418-423.

13. Rossini Aldo. A. Why control blood glucose levels? *Archives of surgery*.1976; 111:229- 238.

14. Posthauer, \ Ellen M .Diet, Diabetes, and Wound Management: How Important is Glycemic Control? *Advances in skin and wound care*. 2004; 3.

15. Jacober JS, Sowers JR. An update on the peri-operative management of diabetes. *Archive of Internal Medicine*.1999;159:2405- 2411

16. Carson JL, Scholz PM, Peterson ED, Gold J, Schneider SH,Diabetes mellitus increases short term mortality and morbidity in patients undergoing coronary artey bypass graft surgery. *American College of Cardiology Foundation* 2002; 40:418-23.

17. Guvener M, Pasaoglu, Demircin M,Perioperative hyperglycemia is a strong correlate of postoperative infection in typeII diabetic patients after CABG. *Endocrine journal.*2002;49:531-537.

18. Hirsch IB, Paauw DS, Brunzell J. Inpatient management of adults with diabetes. *Diabetes Care* 1995; 18: 870-878.

19. Alberti KGMM, Sherwin, Stamford, Appleton, Lange .Diabetes and surgery. [editorial] Anesthesiology 1991; 209.

20. McMurray JF. Wound healing with diabetes mellitus. Surgical clinics of North America 1984:64:769-78

21. Gavin LA: Peri-operative management of the diabetic patient. *Endocrinology and Metabolism Clinics North America* 1992; 21: 455-75.

22. Hirsch IB, Paauw DS, Diabetes management in special situations. *Endocrinology and Metabolism clinics of North America* 1997; 26:631-645.

23. Pomposelli JJ, Baxter JK III, Babineau TJ, Pomfret EA, Driscoll DF, Forse RA, Bistrian BR: Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. *Journal of Parenteral Enteral Nutrition*1998; 22:77– 81.

24. Tepper OM, Capla JM, Galiano RD, Ceradini DJ ,Gurter GC, Adult vasculogenesis occurs through in situ recruitment, proliferation, and tubulization of circulating bone marrow– derived cells. *Blood.*2005; 105:1068–1077.

25. Hanahan D. Signaling vascular morphogenesis and maintenance. Science. 1997; 277:48–50.

26. Xueliang , Edelstein D, Obici S, Higham N, Brownlee M. Insulin resistance reduces arterial prostacyclin synthase and eNOS activities by increasing endothelial fatty acid oxidation. *Journal of Clinical Investigation.*2006;116:107-1080 .

27. Bhatia JY, Pandey K, Rodrigues C, Mehta A, Joshi VR. Postoperative wound infection in patients undergoing coronary artery bypass graft surgery. *Indian Journal of Medical Microbiology* 2003; 21:246-251.

28. McAlister FA, Man J, Bistriz L, Amad H, Tandon P. Diabetes and coronary artery bypass surgery; *Diabetes care* 2003; 26:1518-1524.

29. Gandhi GY, Nutall GA, Abel, Mullany CJ, Willam BA, McMohan MM. Intra operative hyperglycemia and peri-operative outcomes in cardiac surgery Patients. *Mayo Clinical proceedings.* 2005; 80:862-866.

30. Malmberg K**.** Prospective randomized study of intensive insulin treatment on long-term survival after acute myocardial infarction in patients with diabetes mellitus. *British Medical Journal*.1997;314:1512-151

31. Krinsley JS. Effect of intensive glucose management protocol on the mortality of critically ill adult patients. *Mayo Clinic Proceedings*. 2004; 79:992-1000.

32. Pittas AG, Siegel RD, Lau J. Insulin therapy for critically ill hospitalized patients: a meta- analysis of randomized, control trials. *Archive of Internal Medicine*. 2004; 164:2005-2011.

33. Milaskienicz Z RM, Hall GM: Diabetes and anaesthesia. *British Journal of*

Anaesthesia 1992; 68: 198-206.

34. Rassias AJ, Marrin CA, Arruda J, Whalen PK, Yeager MK.Insulin infusion improves neutrophil function in diabetic cardiac surgery patients*: Anesthesia Analgesia* 1999;88:1011–6.

35. Lazer HL, Chipkin SR, Fitzgerald CA, Cabral H Apestin CS . Tight glycemic control in diabetic coronary artery bypass graft patients improve peri operative outcomes and decreases recurrent ischemic event; *Circulation*. 2004; 109:1497-1502.

36. The Diabetes Control and Complications Trial Research Group. The effect of intensive diabetes therapy on the development and progression of Neuropathy. *Annals of Internal Medicine* 1995;122:561-8.

37. Ian Peacock. Glycosylated haemoglobin: measurement and clinical use. *Journal of Clinical Pathology* 1984; 37:841-851.

38. Giugliano D, Ceriello A, Paolisso G. Oxidative stress and diabetic vascular complications. *Diabetes Care* 1996; 19:257- 67.

39. Baynes JW. Role of oxidative stress in development of complications in diabetes. *Diabetes* 1991; 40:405-12.

40. Hennesse PJ, Ford EG, Black T, Andrassy RJ. Wound collagenase activity correlates directly with collagen glycosylation in diabetic rats. *Journal of pediatric*

surgery.1990: vol. 25: 75-78.

41. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Annals of Internal Medicine* 2004; 141:421- 31.

42. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N**,** Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European Prospective Investigation into Cancer in Norfolk. *Annals of Internal Medicine*.2004; 141:413 420.

43. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. *New England Journal of Medicine*. 1993; 329:977-86.

44. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. *Lancet.* 1998; 352:837-53.

45. Bishop JR,Moul JW,Sihelnik SA,Peppes DS,GormellyTS, McLeod DG.Use of glycosylated hemoglobin to identify diabetics at high risk for penile peri-prosthetic infections.*Journal of urology* .1992; 147:386-388

46. Wilson SK, Carlson CC, Cleaves MK, Delk .Quantifying risk of penile prosthesis infection with elevated glycosylated haemoglobin. *Journal of urology.* 1998;159: 1537-1539.

47. Puskas F, Hilary P. Grocott, White WD, Mathew JP, Newman MF, Yosef SB, Intra-operative hyperglycemia and cognitive decline After CABG *Annals of Thoracic Surgery* 2007;84:1467-1473**.**

48. Hostetter MK. Handicaps to host defense. Effects of hyperglycemia on C3 and Candida albicans *Journal of Thoracic Cardiovascular Surgery* 2000; 119:108-114.

49. Yue DK, McLennan S, Marsh M, Mai YW, Spaliviero J, Delbridge L, Reeve T , Turtle , Effects of experimental diabetes, uremia, and malnutrition on wound healing . *Diabetes,* 1987; 36:295-299.

50. Bagdade JD, Stewart M and Walters E**.** impaired granulocyte adherence. A reversible defect in host defense in patients with poorly controlled diabetes. *Diabetes* 1978; 27: 677-681.

PROFORMA

NAME AGE/SEX WEIGHT

HOSPITAL.NO. DATE OF SURGERY

DIAGNOSI
TYPE OF SURGERY

DATE OF ADMISSION

DURATION OF SURGERY

DURATION OF DIABETES

TREATMENT OF DIABETES OHA/ INSULIN

ASSOCIATED DISEASES

OTHER DRUGS

TYPE OF ANAESTHESIA

PRE- OP BLOOD GLUCOSE Fasting -
Post-prandial -

HbA1C

PRE-Induction
(On the day of surgery)

ANTIBIOTICS:
PRE-OPERATIVE Yes / No
POST-OPERATIVE Yes / No
DURATION OF HOSPITAL STAY -

INTRA-OPERATIVE

	Glucose	Insulin

Ist HOUR		
IInd HOUR		
IIIrd HOUR		
IVth HOUR		

Maintain intraop blood glucose < 140mg.dL-1

POST-OPERATIVE

COMPLICATIONS	Day1	Day2	Day3	Day4	Day5	Day6	Day7
Wound Infection Wound Dehiscence							
Postoperative Blood Glucose							
Post operative ICU stay							
Wound re-exploration							
Hypoglycemic episodes Metabolic derangements							
Cardiovascular events :							
Infections: UTI/RTI							

PATIENT INFORMATION

Person who are diabetic have been shown to be more prone to complications after their surgery such as wound infection, longer hospital stay etc.This has usually been attributed to high blood sugar during and after the surgery .Hence we check blood sugar at frequent interval and take measures to correct it

There has been concern that long term control of sugar, may also contribute to these complications. Glycosylated hemoglobin reflects the control of sugar over the previous 2-4 months. This study is an attempt to look into this aspect. We want to see if the complications are less in patients with high Glycosylated hemoglobin, if the blood sugar is maintained lower than what is usually maintained after surgery i.e., around 140mg instead of less than 200mg.If you volunteer for this study, we would be taking a blood sample to check your Glycosylated hemoglobin if not done with in the last one month. However volunteering for this study is optional and the care that you receive in this hospital will not be affected by your decision

INFORMED CONSENT

I have been explained in detail about the study by dr. ----------

I am willing to volunteer at my own free will and am aware that I can withdraw at any time, without it affecting my medical care in this hospital.

Doctors name: signature:

Signature:

S/NO.	H.NO	AGE	GROUP	SEX	WEIGHT	TYPSX	SXD	DODM	OT PROB	TY OF AN	PRE
1	989987 C	68	1	1	57	1	630	3	1	1	
2	449257 B	54	1	1	56	2	360	20	5	1	
3	980435 C	55	1	2	65	0	135	10	1	1	
4	873300 A	55	1	2	64	3	150	3		1	
5	998428 C	68	1	2	65	4	120	2	1	1	
6	949625 C	64	1	1	65	5	180	2	1	1	
7	645498 B	65	1	1	65	3	390	7	1	1	
8	507116 C	46	1	1	60	0	150	3	1	1	
9	971043 C	40	1	1	75	0	120	1	1	1	
10	643909 A	59	1	1	60	2	420	18	5	1	
11	036840 D	42	1	1	83	5	120	5		1	
12	012776 D	50	1	1	66	0	660	5		1	
13	016223 D	57	1	1	92	3	120	10	1	2	
14	440373 A	48	1	2	85	3	120	10	1	2	
15	022011 D	43	1	1	45	0	300	5	1	3	
16	017611 D	46	1	1	60	0	240	5		3	
17	929580 C	42	1	2	56	4	150	2		1	
18	154185 A	45	1	2	63	4	120	10	1	1	
19	055135 D	50	1	2	75	4	180	2		1	
20	045528 D	46	1	1	68	3	120	9	1	1	
21	669143 C	57	1	2	72	3	180	1		1	
22	072117 D	48	1	2	68	3	120	5	1	2	
23	820200 C	38	1	2	90	3	150	8	3	2	
24	060622 D	48	1	2	60	3	120	10	1	1	

25	072317 D	56	1	1	56	6	180	6	1	1
26	917291 A	63	2	2	57	3	120	5	5	1
27	008780 D	38	2	2	83	3	240	1	1	2
28	988788 C	42	2	2	50	5	150	3		1
29	988038 C	58	2	1	50	2	390	15	5	1
30	004960 D	64	2	1	68	8	120	22	4	1
31	585833 C	47	2	1	75	5	240	10		1
32	986249 C	56	2	2	58	7	195	5	1	2
33	991035 C	66	2	2	66	2	360	15	5	1
34	004238 D	52	2	2	68	4	150	4	1	1
35	986450 C	54	2	1	67	0	120	1	1	1
36	052822 C	47	2	1	70	8	360	7		1
37	752086 B	52	2	1	65	7	90	4		1
38	567128 B	66	2	1	66	5	240	10	1	1
39	016919 D	65	2	1	69	5	120	1	4	1
40	043602 D	52	2	2	65	4	135	3		1
41	023079 C	44	2	1	65	3	180	3		3
42	952849 C	48	2	1	59	9	240	1	1	1
43	976633 B	51	2	1	55	0	300	1		2
44	003650 D	51	2	2	78	4	135	8		2
45	636106 A	54	2	1	51	0	420	3		2
46	969865 C	56	2	1	63	2	330	10	5	2
47	780420 C	62	2	2	65	3	135	3	1	2
48	447403 C	55	2	1	60	0	270	6		1
49	013265 D	47	2	2	60	3	120	3	1	1
50	984626 C	60	2	1	95	7	120	10	5	2

D2	D3	D4	D5	D6	D7	HBA1C	PREANT	POSTANT	WDINF	HOSSTAY	DEAH
127	110	129	98	133	145	8.5	0	1	0	10	
165	170	265	177	204	149	7.2	0	1	0	9	
151	168	165	154	144	142	8.2	0	1	0	9	
143	129	135	139	135		8	0	0	0	7	
124	184	173	159			8.3	0	0	0	9	
147	156	135	128	133		7.8	0	0	0	7	
137	129	135	113	116	98	7.8	0	1	0	9	
155	135	121	118	131	130	8.4	0	1	0	10	
128						7.5	0	1	0	3	
168	189	223	121	165	156	7.4	0	1	0	10	
138	121	114				8.7	0	0	0	5	
119	124	114	175	262	261	7.7	0	0	0	19	
134	170	218	138			7.7	0	0	0	8	
140	132	142	129			7.4	0	0	0	10	
116	109	210	155	241	250	9	0	0	0	15	
107	114	136	123			7.7	0	0	0	7	
123						10.6	0	0	0	3	
131	122					11.1	0	0	0	5	
144	115	255	263	256		8.8	0	0	1	7	
121	108	116				9.8	0	0	0	7	
137	136	117	130	143		8.4	0	0	0	6	
107	132					9	0	0	0	7	
136	191	195	170			8.5	0	0	0	7	
154	120	123	126			7.7	0	0	0	6	
122	136	145				8.5	0	0	0	5	
185	212	166	152	122		7	0	0	0	12	
173	180	175	90	88	99	10.7	0	0	1	14	
267	239	181	153	158	110	9.5	0	1	0	9	
206	212	213	225	211	225	7.8	0	1	0	17	
208	205	215	188	217	193	8	0	0	1	16	
238	191	182	165	183	208	12.5	0	1	0	15	
193	189	134	134	97		8.1	1	0	1	15	
216	229	227	146	129	137	8.1	0	1	1	15	
246	176	160	131			8	0	0	0	7	
212	196	187	170			12	0	0	0	6	
188	178					7.5	0	1	0	5	
263						8.8	0	0	0	3	

247	224					8.7	0	0	0	4
178						7.1	0	0	0	3
221	157	158	154	130	113	7.2	0	0	0	9
169	177	213	154			7.5	0	1	0	6
183	134	209	194	136		7.5	0	1	0	8
249	100	188	177	208	146	8.8	0	0	0	16
167	160	144	184			10.8	0	0	0	6
129	183	239	125	157	203	7.2	0	0	0	25
215	220	239	220	248		8.5	0	1	1	18
165	238	212	179			8.4	0	0	0	8
247	212	154	133	150	142	8.7	1	1	1	15
210	220	134	156	169		7.1	0	0	0	6
256	245	165	145			7.5	0	0	1	7

GLOSSARY

TYPSX	TYPE OF SURGERY
SXD	SURGERY DURATION
DODM	DURATION OF DIABETES
OT PROB	OTHER PROBLEMS
TY OF AN	TYPE OF ANAESTHESIA
PRE SUG	PRE OPERATIVE SUGARS
INT SUG	INTRA OPERATIVE SUGARS
POST D1	POST OPERATIVE DAY 1
POST D2	DAY 2
D3	DAY 3
D4	DAY 4
D5	DAY 5
D6	DAY 6
D7	DAY 7
HBA1C	GLYCOSYLATED HAEMOGLOBIN
PRE ANT	PRE OPERATIVE ANTIBIOTIC
POST ANT	POST OPERATIVE ANTIBIOTIC
WD INF	WOUND INFECTION
HOS STAY	HOSPITAL STAY
HYPOG	HYPOGLYCAEMIA
UTI	URINARY TRACT INFECTION
RTI	RESPIRATORY TRACT INFECTION